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(54) Slide treatment apparatus

(57) Slide treatment apparatus comprises a box 1 having a plurality of slide mounting bars 4 extending transversely thereof, rotatably mounted in slots 2. The bars 4 are hollow and are provided with apertures whereby fluid passed along the interior of the bars 4 may be directed onto the surface of microscope slides 24 attached to the bars 4. The bars 4 are rotatable between first, second and third positions wherein the slides are disposed horizontally, inclined downwardly and inclined upwardly respectively. Reagents may be applied to the slides 24 when in their first position and the slides 24 may then be rinsed and drained in the second position.

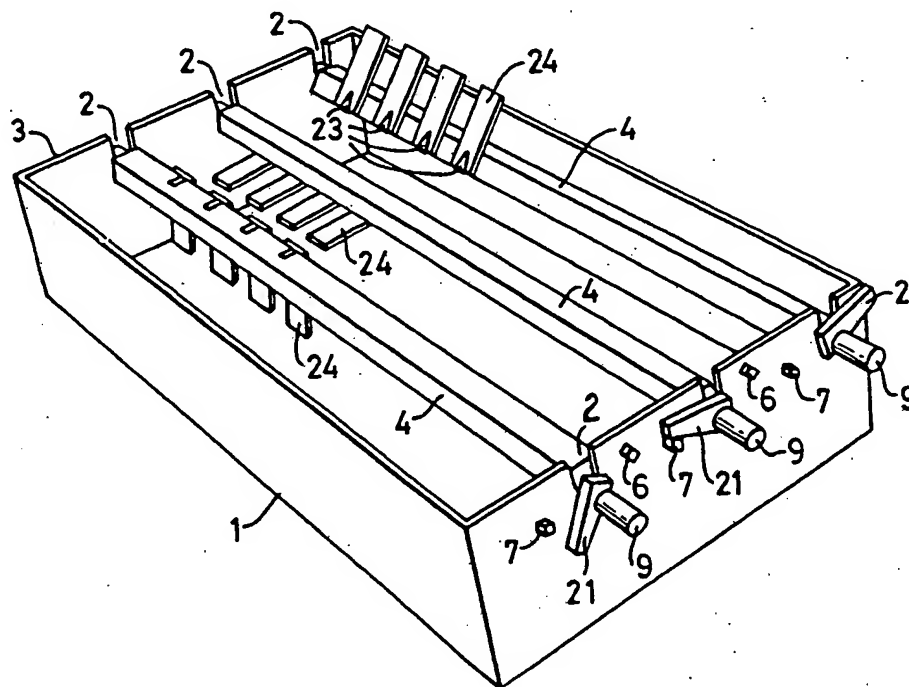


Fig. 1

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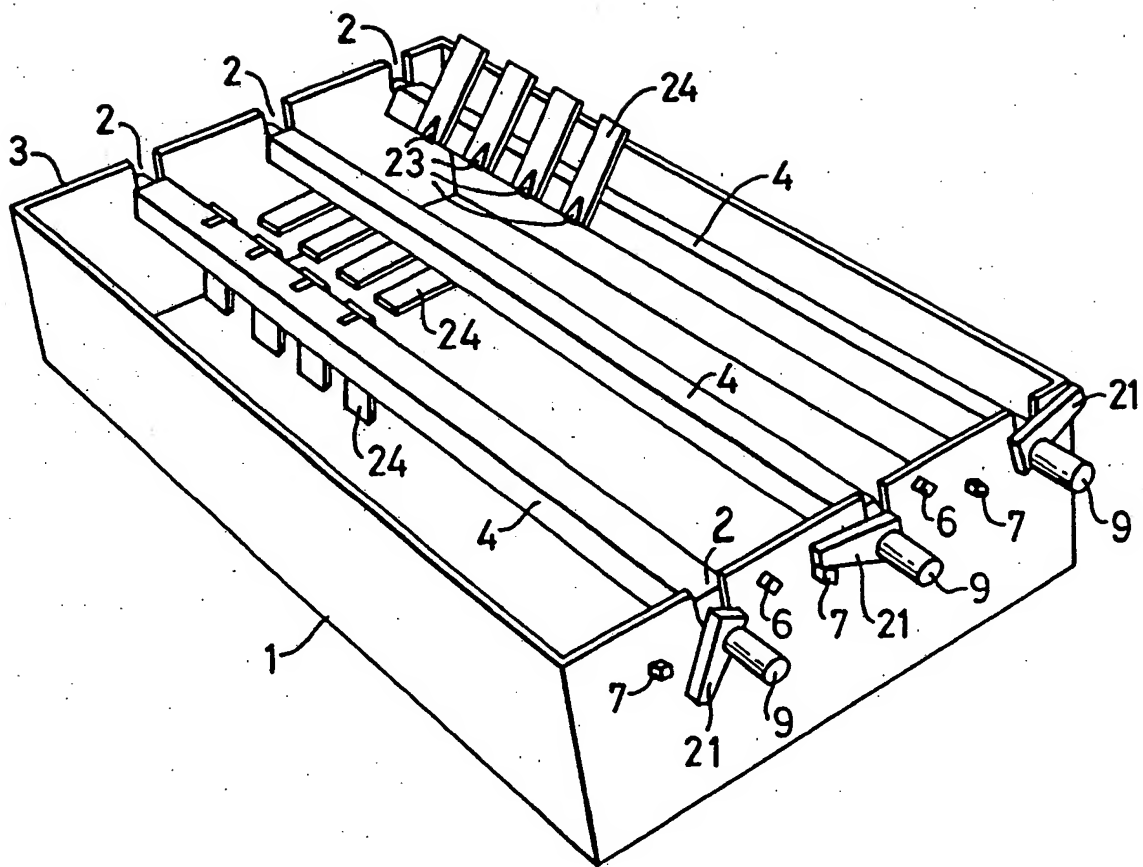


Fig. 1

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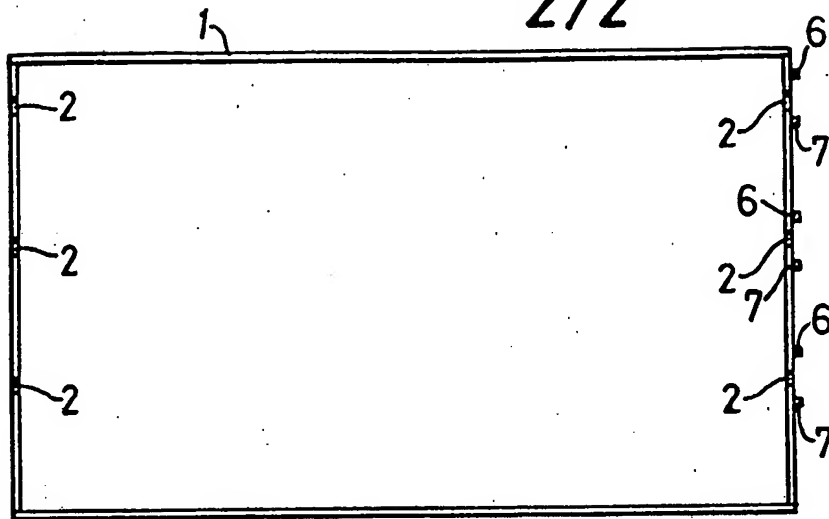


Fig. 2

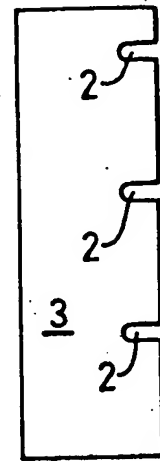


Fig. 3

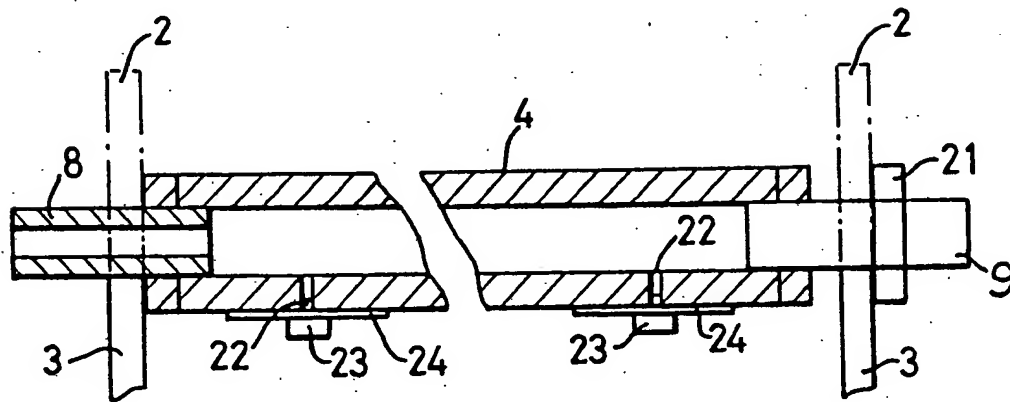


Fig. 4

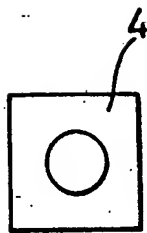


Fig. 5

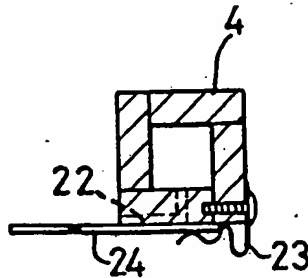


Fig. 7

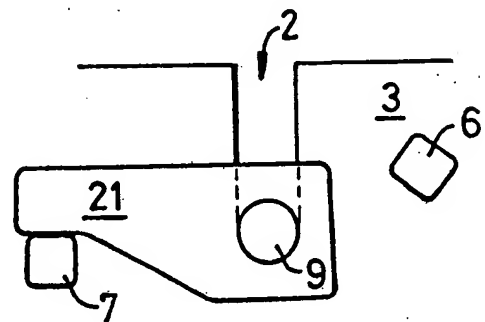


Fig. 6

"SLIDE TREATMENT APPARATUS"

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This invention relates to slide treatment.

There is a need to treat microscope slides carrying biological samples with various materials for purpose such as staining or to obtain reactions to reagents to thereby indicate a particular condition.

Various methods used in the past have involved dipping an entire slide in a reagent solution but this method is not practical if the reagent solution is expensive or if the reagent is available in such small quantities as to make it impractical to consider a solution volume of, say, 100ml containing an acceptable concentration of the reagent.

In the case of certain expensive or scarce reagents it has become common to individually apply a small droplet of reagent in a localized area of the slide and to thereafter rinse slides individually. This is a time consuming and expensive procedure.

A particular example of a method of testing biological samples is immunoperoxidase staining which involves use of certain antibodies which are expensive to produce and which are obtained in small quantities. The antibody is reacted with an antigen in a biological sample and adheres thereto. Thereafter immunoglobulins are applied to the biological sample and a peroxidase indicator system is used.

The present invention seeks to provide slide treatment apparatus which will be useful in applying materials to slides.

The present invention provides microscope slide treatment apparatus comprising a support, a slide mounting means mounted to the support and to which a plurality of slides may be mounted, and liquid delivery means for directing a liquid onto slides mounted on the mounting means; and wherein the slide mounting means is movable with respect to the support between first and second positions in which slides mounted there to extend, generally horizontally and substantially inclined to the

horizontal whereby to enable the slides to be selectively oriented generally horizontally for application thereto of a reagent or substantially inclined to the horizontal for the purpose of rinsing or draining.

5           The slide mounting means preferably includes an elongate member adapted to pivot about an axis between said first position and said second position.

10           The slide mounting means preferably carries an abutment adapted to engage with first and second abutments carried by said support for defining said first position and a third position.

          The slide mounting means preferably includes a plurality of clips for holding slides.

15           The slide mounting means preferably carries at least part of said liquid delivery means.

          In a preferred instance the slide mounting means includes a hollow tube having apertures therethrough oriented to pass liquid onto slides carried by the slide mounting means. In this instance, the hollow tube may  
20           be connected to a source of liquid such as a rinsing liquid. Such connection may be achieved by a tube or by a channel in which the hollow tube is located.

          In an alternative, the liquid delivery means is provided by a channel, a plurality of tubes or spray  
25           means.

          The slide mounting means is preferably mounted above a container adapted to catch liquid, which may run off from the slides.

          A lid for that container may be provided.

30           In another aspect the present invention provides a microscope slide having an upstanding ridge extending thereacross comprised of a water repellent material which is not soluble in dewaxing solvents. A suitable material is polytetrafluoroethylene. Such a ridge  
35           preferably has a width of about 2mm.

A specific construction of microscope slide treatment apparatus in accordance with this invention will now be described with the aid of the accompanying drawings in which:

5           Fig. 1 is a perspective view of the apparatus,  
            Fig. 2 is a plan view of a box forming part of the apparatus,

            Fig. 3 is a side elevational view of the box of Fig. 2,

10           Fig. 4 is front elevational view of a slide holder bar,

            Fig. 5 is a view of one end of the bar of Fig. 4,

            Fig. 6 is a view of the other end of the bar of Fig. 4, and

15           Fig. 7 is a cross-sectional view of the bar of Fig. 4.

The apparatus shown in the drawings comprises a box 1 formed of acrylic. A lid (not shown) may be provided for the box.

20           The box 1 has a drain outlet (not shown) and a plurality of slots 2 formed in its opposed end walls 3 in which slide mounting bars 4 are received.

            One of the end walls 3 carries a plurality of abutments 6 and 7 arranged adjacent the slots 2.

25           The bars 4 are square in section and are hollow, and have a tubular portion 8 extending from one end thereof, which communicates with the hollow interior of the bar 4, and a solid rod portion 9 extending from the opposite end, the tubular and rod portions 8 and 9  
30           resting in the slots 2 in use. The bars 4 may thus be rotated about their longitudinal axes between first and third positions defined by a radially extending arm 21 which engages the abutments 6 and 7 formed on one of the end walls 3. A plurality of spring clip means 23 are  
35           provided, spaced along the length of each of the bars 4,

to which microscope slides 24 may be affixed to extend outwardly from the bar 4. As shown in Fig. 1, the right hand bar 4 is in its third position with the slides 24 inclined upwardly, the centre bar 4 is in its first position with the slides 24 extending generally horizontally, and the left hand bar 4 is in its second position with the slides 24 extending downwardly. This second position may be selected by sliding the bar 4 axially such that the arm 21 may be rotated clear of the abutments 6 and 7.

A plurality of apertures 22 are formed in one face of the bar 4 adjacent each of the clip means 23. In use, the tubular portion 8 will be connected to a source of fluid, such as an irrigating liquid, via a tube fitted with a tap, such that the fluid may pass into the hollow interior of the bar 4 and exit via the apertures 22 onto the surface of the slides 24 mounted in the clips 23.

In use, the third (upwardly inclined) position allows the slides 24 to be mounted and air to be displaced from the system. The first (horizontal) position allows irrigation of samples (sections) on the slide and the application and incubation of reagents, and the second (downwardly inclined) position allows the irrigating fluid to be drained from the slides 24.

The above described apparatus has been found to be of particular use in immunoperoxidase staining using generally the techniques described by

Sternberger L.A., (1974), Immunocytochemistry. Englewood Cliffs, N.J., Prentice Hall. Heyderman E. (1979). Immunoperoxidase technique in histopathology: applications, methods and controls. J. Clin. Path., 32, 971-978, or Bourne J.A. (1983), Handbook of immunoperoxidase staining methods. Santa Barbara C.A. Dako Corporation.

A particularly preferred procedure is set out below.

Slides are attached to the clip means 23 of the bars 4 after blocking endogenous peroxidase. In order to rinse the slides they are flooded with irrigation fluid, drained, flooded again and left in the horizontal position for 5 minutes and the process repeated. The slides are then drained and whilst in the downwardly inclined position the lower end of the slide is touched with a rolled up tissue to absorb most of the remaining fluid. The slides are then placed in the generally horizontal position. If the whole slide is still wetted in continuity with the moisture on the section, the section can be isolated using a small camel hair brush soaked in acetone and so allow localisation of reagents on the section rather than spreading over the slide. Mounting sections towards one end of the slides rather than in the centre facilitates this. After the chromogen stage the slides are replaced in the carrier for counterstaining, dehydration and clearing. Initially, phosphate buffered saline (PBS) was used as the irrigating fluid but we have found that 0.9% NaCl in tap water gives indistinguishable results. Bovine serum albumin in PBS remains the diluent for the immunoglobulins.

Many hundreds of sections have been stained with the above apparatus and overall results have been excellent. We are able to process 48 sections at a time and still save 40 minutes on the time previously taken for 33 sections. To formally assess the new apparatus 40 pairs of slides were simultaneously processed, one from each pair in the traditional box and the other in the above apparatus. The same batches of reagents were used for both boxes. After processing, each slide of the pair was given a randomisation code prior to scoring by 3 independent observers. The first slide of each pair was then assessed for intensity of staining and rated as staining better, the same as or worse than its fellow.



The randomisation code was then broken and the non-parametric Sign Test applied to the data.

5 Of the 40 pairs of slides 39 pairs were available for comparison, one section having been lost in the traditional box. Of the 117 pair assessments, 60 pairs were scored the same, in 35 the traditional box was preferred and in 22 the above apparatus was preferred. The Sign Test applied to this data gave a 2 tailed p value of 0.25 indicating no significant difference in the  
10 quality of staining from the boxes.

Finally a small experiment was set up to test the effect of acetone on the staining protocol. Five pairs of slides were used, one of each pair being processed with the usual diluent containing 10% acetone. Acetone  
15 had no effect on the quality of staining.

The results we have obtained with the above apparatus indicate that it is capable of greatly reducing the time taken to process large numbers of slides whilst retaining a high degree of quality. The  
20 above apparatus could be constructed for any number of slides but is increasingly worthwhile when a dozen or more slides are processed.

Other advantages are the rinsing of chromogens of dubious safety before touching the slides and the loss  
25 of fewer sections from the slides. We believe that the utility of this equipment will find wide appeal amongst clinical pathologists and research workers.

Since the above treatment with acetone to disperse water is somewhat tedious, we now prefer to use slides  
30 having an about 2mm wide ridge of polytetrafluoroethylene to contain reagents against dispersal.

Since modifications within the spirits and scope of the invention may be readily effected by persons skilled in the art, it is to be understood that the  
35 invention is not limited to the particular embodiment described, by way of example, hereinabove.

## Claims

1. A microscope slide treatment apparatus comprising support means, slide mounting means adapted to be mounted upon said support means and to which a plurality of slides may be mounted, and liquid delivery means adapted to direct a liquid onto slides mounted on the mounting means; and wherein said slide mounting means is movable with respect to said support means between at least first and second positions such that, when in said first position, slides mounted on said mounting means are disposed substantially horizontally and, when in said second position, are substantially inclined to the horizontal.
2. Apparatus as claimed in claim 1 wherein said slide mounting means includes an elongate member adapted to pivot about its long axis between said first and second positions.
3. Apparatus as claimed in claim 2 wherein said elongate member is provided with means for engaging the edges of a plurality of slides spaced along the length thereof.
4. Apparatus as claimed in claim 2 or claim 3 wherein said elongate member is provided an abutment member adapted to selectively engage a plurality of cooperating abutment members arranged on said support means thereby defining said first position and a third position.
5. Apparatus as claimed in any of claims 2 to 4 wherein said elongate member is hollow and is provided with a series of apertures along its length whereby liquid may pass along said hollow member and exit through said apertures onto slides mounted on said elongate member.
6. Apparatus as claimed in claim 5 wherein said hollow member is connectable to a source of liquid.
7. Apparatus as claimed in any of claims 1 to 4 wherein said liquid delivery means is provided by a channel, a plurality of tubes or spray means.
8. Apparatus as claimed in any preceding claim wherein said slide mounting means is mounted above a

container adapted to catch liquid drain from said slides.

9. Apparatus as claimed in claim 8 wherein said container serves as said support means.

5 10. Apparatus as claimed in claim 9 wherein said slide mounting means is rotatably mounted in a pair of slots formed in opposed walls of said container.

11. Apparatus as claimed in claim 10 wherein a plurality of slide mounting means are provided in spaced parallel series across the width of the container.

10 12. Apparatus as claimed in any of claims 8 to 11 wherein said container is provided with a lid.

13. Apparatus as claimed in any of claims 4 to 12 wherein said slides, when said slide mounting means is in second position, are inclined downwardly and, when in said  
15 third position, are inclined upwardly.

14. A microscope slide treatment apparatus substantially as hereinbefore described with reference to the accompanying drawings.